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Imaging is used in virtually every cancer patient, in many animal models of cancer, and in a large number of in vitro cancer-related experiments. Imaging research is thus fundamental to advanced cancer research. The medical physics program at the University of Chicago is recognized internationally for its research excellence and for its training of investigators at the pre-doctoral and post-doctoral level. Many of the trainees go on to careers in cancer research. We believe that exposure and immersion of undergraduate students in summer research in breast cancer imaging is expected to provide a forum for establishing a set of next-generation researchers who will pursue breast cancer research via Ph.D. or Ph.D./M.D. programs as their career. Six undergraduate students participate in research in breast cancer imaging at the University of Chicago within the laboratory and administrative structure of the well-established Graduate Programs in Medical Physics. Six summer students in the Summer 2004 quarter learned and experienced research in breast cancer imaging through didactic lectures, hands-on research, interactive research project meetings, formal research seminars, and in the writing and oral presentation of their research. All four of the mentors who participated as primary summer advisors in the grant (Giger, Halpern, Jiang, and Nishikawa) have a long history of breast cancer research and funding.

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Summer Undergraduate Research Training in Breast Cancer Imaging

INTRODUCTION

Imaging is used in virtually every cancer patient, in many animal models of cancer, and in a large number of in vitro cancer-related experiments. Imaging research is thus fundamental to advanced cancer research. The medical physics program at the University of Chicago is recognized internationally for its research excellence and for its training of investigators at the pre-doctoral and post-doctoral level. Many of the trainees go on to careers in cancer research. We believe that exposure and immersion of undergraduate students in summer research in breast cancer imaging is expected to provide a forum for establishing a set of next-generation researchers who will pursue breast cancer research via Ph.D. or Ph.D./M.D. programs as their career. Six undergraduate students participate in research in breast cancer imaging at the University of Chicago within the laboratory and administrative structure of the well-established Graduate Programs in Medical Physics. Six summer students in the Summer 2004 quarter learned and experienced research in breast cancer imaging through didactic lectures, hands-on research, interactive research project meetings, formal research seminars, and in the writing and oral presentation of their research. All four of the mentors who participated as primary summer advisors in the grant (Giger, Halpern, Jiang, and Nishikawa) have a long history of breast cancer research and funding. In addition, the summer students have attended research presentations of others in the labs (such as post-doctoral fellows, graduate students, and faculty) and each presented their research at the end of summer to researchers at the University of Chicago.

ACCOMPLISHMENTS

Six students participated in the summer undergraduate training in breast cancer imaging during the Summer of 2004. Each student was assigned to one of the four investigators on the grant (Giger, Nishikawa, Jiang, or Halpern) and performed research in their lab. In addition, the students participated in day tours to other faculty labs as well as in clinical areas such as breast MRI, diagnostic breast imaging, and CT. The students' research and accomplishments are listed below for each student.

1. Brian Frisch, DePaul University (Advisor: R. Nishikawa)

Brian assisted in Dr. Nishikawa's research in developing computer-aided detection of mass lesions in digital breast tomosynthesis (DBT) images. DBT is a new radiographic technique for breast imaging. Multiple 2D projection images are made at different angles and these projection images are then reconstructed to form 3D image of the breast. Specifically Brian developed a method to segment breast lesions from the 3D image set. The segmentation consisted of a difference of Gaussian filters followed by a top hat transformation. This approach has been used on conventional mammograms by other groups. The result of this approach was compared to another approach developed in our lab that measures gradients in the image. The gradient method proved to be superior. Brian learned about computer-aided diagnosis, x-ray imaging of the breast, specifically DBT, different image processing techniques, evaluation of computer-aided detection schemes, and how to program in Matlab. His results, will being negative, gave us confidence that the approach that we are using has advantages over other approaches.

2. Steven Jaditz, University of Chicago (Advisor: H. Halpern)

Steve Jaditz came to Dr. Halpern's with considerable expertise and experience with high level programming, and expressed an interest in applying this to needs within our group. We are developing a novel imaging technology to provide quantitative oxygen images in living tissues with electron paramagnetic resonance, EPR. The oxygen images are derived from four dimensional spectral spatial images of a spin probe that reports the local oxygen concentration from the width of its EPR spectral line. The heart of our technology is based on an algorithm to extract highly accurate spin packet line widths from a line broadened by instrumental conditions including Zeeman field modulation and irradiation power. The graphical user interface (GUI) is based on a legacy version of MATLAB and does not take advantage of the modern interfaces provided by updated versions of MATLAB. We also were uncomfortable with the parametric error estimations provided by the algorithm and needed to test this aspect of the program.

Steve completely rewrote the GUI in modern MATLAB for the program, a very difficult task. It is still in the testing and modification stage but, with our next summer student should find its way into the laboratory tool box. He also has completed his analysis of the error estimation algorithm and found a fundamental flaw in it. We have modified the standard algorithm to reflect this flaw and have found an improved association of parametric error estimates and the variance of parameters from repeated experiments.

2. David Lee, Duke University (Advisor: H. Halpern)

David was an undergraduate from Duke University interested in physics and medicine, and very willing to join in the effort of our group to validate the oxygen measurements displayed in our high resolution EPR oxygen images. David rapidly involved himself in learning how to operate the EPR spectroscopic imager, which involved learning about the fundamentals of the EPR experiment, and basics of projection derived images. David was heavily involved in the development of an experiment using an Oxylite fiberoptic oxymeter mounted in a sterotactic stage. By locating fixtures that could be identified in the oxygen image with the stereotactic stage, the oxygen values along tracks measured with the Oxylite probe could be related to voxels within the EPR oxygen image. The results from this work beautifully corroborated the oxygen measurements in the EPR image. David's hard work and creative approach to the experiment and its analysis earned him authorship on the paper describing this work.

2. Philip Smithback, University of Chicago (Advisor: Y. Jiang)

Philip Smithback is a physics-major college student at the University of Chicago. He embarked on a research project investigating the effect of reader inattention on receiver operating characteristic (ROC) analysis. ROC analysis is widely used in radiology research to measure reader performance in observer tasks such as lesion detection in anatomical images. Generally, when ROC data is collected in an experiment, the observer is put under a test condition. The observer is usually fully attentive to the observer task at hand, perhaps even more so than when the observer performs the same task outside of the test condition, when inattention can occur inadvertently. The purpose of this project was to investigate whether reader inattention causes anomalies in ROC analysis when it occurs in an ROC experiment.

Philip implemented an experiment designed by Dr. Jiang for this project. To do this, Philip acquired a working knowledge of the C^{++} programming language and read on the topic of ROC analysis, particularly the mathematical aspects of it. He then wrote computer programs implementing the experiment. Specific functions that he implemented include generating and displaying an image, creating Gaussian-distributed noise in the image, creating simple, specified geometric shapes in the image, and filling a geometric shape with a constant pixel value,

etc. During the summer project, Philip successfully completed implementing the experiment, and participated in the initial reader studies of this experiment. This experiment was later used in work published as a proceeding paper in the SPIE's Medical Imaging 2005 Symposium.

In addition, Philip also worked on another project in which the relationship between the softcopy display of low-contrast lesions and their detectability is investigated. Philip wrote computer programs that allow one to manipulate the display of images. However, this project was not completed when the summer came to an end. This project is currently pending further work.

During the summer, Philip attended many seminars and workshops that taught him about the research and applications of Computer Aided Detection and Computer-Aided Diagnosis (CAD). He acquired a wealth of information about breast CAD in particular, which was the specific area he participated in research, and experienced the process of breast cancer diagnosis in both clinical and research areas.

2. <u>Meena Anand, Princeton University (Advisor: Y. Jiang)</u>

Meena Anand is a psychology-major college student at Princeton University. She worked on a project in collaboration with a medical student at the University of Chicago to evaluate a computer-aided diagnosis technique. The computer-aided diagnosis technique was developed previously at the University of Chicago. It analyzes digital mammograms that contain clustered calcifications and estimates the likelihood of malignancy for the lesion. A radiologist could use this information in deciding whether to recommend biopsy for the lesion. Various evaluations have already been carried out for this technique in the past; the purpose of this summer research project was to evaluate the computer technique on calcifications that were considered by a radiologist as safe to follow-up and, thus, not recommended for biopsy. It is important that the computer technique does not yield a high estimate of the likelihood of malignancy for lesions that are confirmed to be benign through long-term follow-up.

In this project, Meena and the medical student collected a database of cases with calcifications that were considered clinically by a radiologist as safe to follow and not recommended for biopsy. They identified candidate cases from reading a large collection of radiology reports. Subsequently they retrieved the digital images from the Radiology Picture Achieve and Communication System. They then processed these images (changing their size, pixel value, identifying the lesions, etc.) so that they can be used for research analysis. Next they retrieved pathology reports of select cases when necessary. They then reviewed the cases that appear to be appropriate for the study with Dr. Jiang and further

reduced the case pool. Finally, they used the computer technique to analyze the cases that they collected. The computer technique was designed to be interactive in a way that improper use by a reader could adversely affect the results of the computer analysis. Therefore, familiarization with the computer technique and repeated analysis using the computer technique ensued. The intent of this research project was to conduct an observer study with radiologists serving as observers. The research did not progress sufficiently to carry out the observer study at the end of the summer research period. This project is currently pending and will be merged with a larger-scale evaluation project.

In addition to research, Meena attended seminars and workshops in the summer. She learned about the research and applications of Computer Aided Detection and Computer-Aided Diagnosis (CAD). She experienced the process of breast cancer diagnosis in both clinical and research settings.

2. Nick Gruszauskas, University of Illinois at Chicago (Advisor: M. Giger)

The field of computer-aided diagnosis (CAD) is rapidly growing, especially in the area of the detection and diagnosis of lesions in breast images since the earlier breast cancer is found the better the prognosis for the patient. While in Dr. Giger's lab, Nick increased his knowledge of medical imaging through the reading of books on breast imaging, image processing, and medical physics, and through various discussions with me and others in the lab. He learned about scientific investigations and the corresponding need for creativity and rigor.

In the lab, Nick first helped in the collection of sonographic breast images but he then quickly became immersed in the sonographic image analysis aspect as a major contributor. Due to his efforts, we are now able to translate our computer-aided diagnosis workstation for ultrasound to the clinical breast imaging area of the Department of Radiology. Nick developed and implemented a method for automatically estimating the pixel size of any clinical ultrasound image, thus allowing our CAD software to run on the fly. This method required knowledge of the ultrasound image, matched filtering methods, and programming methods. He also worked with others in the lab, as well as with one of clinical mammographers, to design a user-friendly clinical interface for the sonographic workstation and then integrate it with the Radiology PACS system.

Nick presented his research on the technical aspects that allow for the clinical translation of sonographic breast CAD at the annual SPIE meeting on Medical Imaging in San Jose, California– one of the premier meetings for medical imaging scientists and engineers.

KEY RESEARCH ACCOMPLISHMENTS

1. An ongoing summer undergraduate research program in breast cancer imaging has now been established at the University of Chicago, under the direction of M. Giger who also directs the graduate programs in medical physics.

2. The competitive program is limited to 6 undergraduate slots per summer and has successfully trained 6 students during the summer of 2004.

3. Undergraduate students are learning the rigors of research and are contributing to a level that allows for co-authorship on presentations and future papers.

4. Evidence of the influence of the program is shown through the education/career choices of the 2004 summer students with N. Gruszauskas considering MD/PhD programs in radiological imaging and others in medical physics and biomedical engineering.

REPORTED OUTCOMES

1. **N. Gruszauskas**, K. Drukker, and M. L. Giger. "Character recognition and image manipulation for the clinical translation of CAD for breast ultrasound," Proceedings of SPIE Medical Imaging 2005 Vol 5747.

CONCLUSIONS

We have established a formal summer undergraduate research program in breast cancer imaging at the University of Chicago. The students are being exposed to various laboratories and clinical areas as well as being immersed in a focused research project. They also have attended various presentations by post-doctoral fellows, graduate students, and faculty during the summer. The six summer students in the Summer 2004 quarter learned and experienced research in breast cancer imaging through didactic lectures, hands-on research, interactive research project meetings, formal research seminars, and in the writing and oral presentation of their research. All four of the mentors (Giger, Halpern, Jiang, and Nishikawa) participated as primary summer advisors in the grant.

With the start of summer 2005, we received multiple applications for the summer undergraduate research training program, however we have accepted only six for the funded slots.